

PERGAMON PRESS

OXFORD · LONDON · EDINBURGH · NEW YORK
TORONTO · PARIS · FRANKFURT
1966

ADAPTATION TO CO₂ WITH PARTICULAR RELATION TO CO₂ RETENTION IN DIVING

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Abstract — Adaptation to CO₂ produces a typical breathing pattern of increased tidal volume and lowered respiratory rate. Anatomical and physiological deadspace, as well as arterial-alveolar CO₂ and O₂ gradients, are increased under these conditions. The relationship of these findings with the well known lowered respiratory response to high CO₂ concentrations after CO₂ adaptation is discussed. Evidence for CO₂ adaptation in routine diving is presented.

Zusammenfassung — Die Anpassung an längerdauernde Kohlensäure Einwirkung äussert sich in einem typischen Atmungsrythmus mit erhöhtem Atemvolumen und verminderter Atemfrequenz. Der anatomische und physiologische Totraum ist vergrössert und der AaD_{CO} und AaD_O erhöht. Die Beziehung dieser Befunde zu der bekannten verminderten Reaktion der Atmung bei Einatmung hoher CO₂ Konzentrationen nach CO₂ — Adaptation wird diskutiert. Es werden Befunde berichtet, die beweisen, dass Kohlensäureadaptation bei regelmässigem Tauchen auftritt.

Résumé — L'acclimatation à l'absorption de CO₂ pour une longue durée se traduit par une augmentation du volume d'air inspiré et une réduction de la fréquence respiratoire. Les temps-morts anatomique et physiologique ainsi que les gradients artériolvéolaires en CO₂ et O₂ sont augmentés. On discute les relations existant entre ces résultats et le fait bien connu que le système respiratoire devient moins sensible au gaz carbonique après acclimatation à l'hypercapnie. Il est en outre démontré qu'il y a adaptation au CO₂ dans le cas de plongées régulières.

IT HAS been established that prolonged exposure to increased CO₂ concentration results in a reduction of the ventilatory response to CO₂ (Haebisch, 1949; Schaefer, 1949; Chapin, 1955). CO₂ tolerance curves obtained after three days of exposure to 3 per cent CO₂ showed a shift to the right and a decrease in slope (Schaefer, 1949). During acclimatization to 3 per cent CO₂, the tidal volume increased and respiratory rate decreased (Schaefer, 1949) which suggested that the respiratory pattern is an important factor in the respiratory response to CO₂. Studies of acute exposure to various CO₂ concentrations on a large group of subjects established clearly the relationship of respiratory pattern and ventilatory response to CO₂. Subjects with a large tidal volume and a low frequency showed a significantly lower response to CO₂ than those with a small tidal volume and high respiratory rate (Schaefer, 1958) (Fig. 1).

Subjects were classified in a low and high ventilation group, using as criteria a ventilation ratio of 4 at 5.4 per cent CO₂ and 6 at 7.5 per cent CO₂. For example,

subjects who responded to the inhalation of 5.4 per cent CO_2 with an increase in respiratory minute volume less than four times the basic volume on air were grouped in the low ventilation group. By comparing the CO_2 tolerance curves of the low and high ventilation groups with those collected under conditions of adaptation to prolonged exposure to 3 per cent CO_2 (Fig. 2), it was concluded that the low ventilation group had to be considered adapted in normal life to a higher CO_2 level.

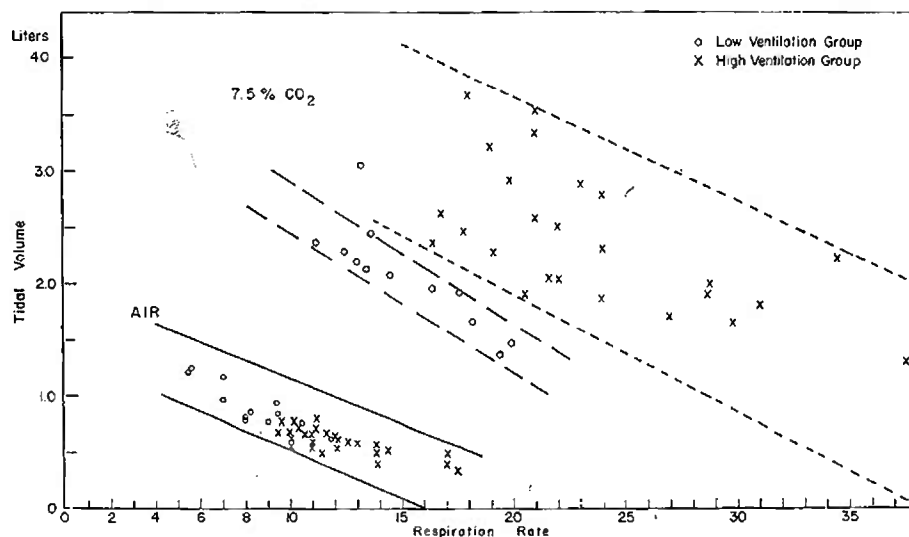


FIG. 1. Relationship between respiratory rate and tidal volume breathing air and breathing 7.5 per cent CO_2
 o Low ventilation group
 x High ventilation group.

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Supporting evidence for this notion was obtained in a study of 21 subjects exposed to 1.5 per cent CO_2 for 42 days (Schaefer *et al.*, 1963). Figure 3 shows changes in respiratory pattern during acclimatization to 1.5 per cent CO_2 . Tidal volume increased markedly throughout exposure and remained high for nine days of recovery, while respiratory rate declined after initial transitory rise. Increase in respiratory minute volume, produced by exposure to 1.5 per cent CO_2 , amounted to 34–38 per cent and was mainly accomplished through change in tidal volume.

Throughout exposure to CO_2 anatomical dead space was increased and alveolar ventilation, expressed in per cent of total ventilation, was correspondingly decreased.

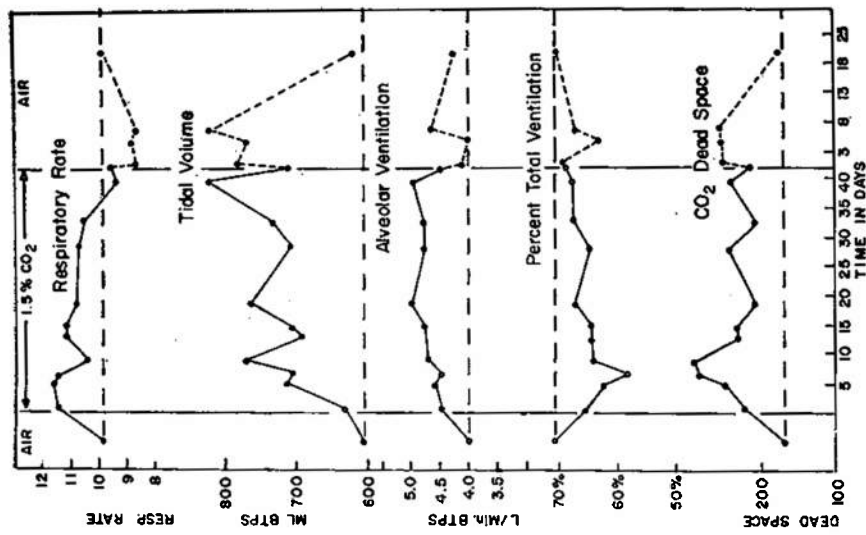


Fig. 3. Effect of prolonged exposure to 1.5 per cent CO₂ on respiratory rate, tidal volume, alveolar ventilation and anatomical dead space. (Mean values 21 subjects). Printed with permission of the *Journal of Applied Physiology*

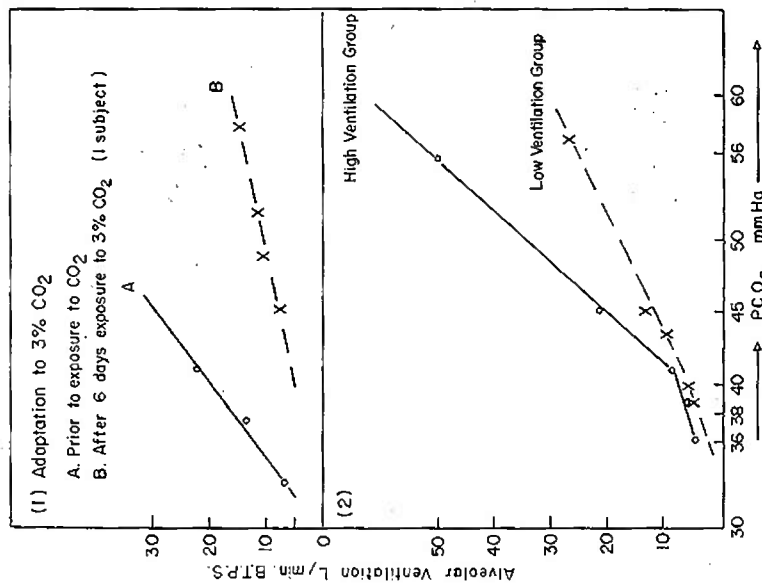


Fig. 2. CO₂ ventilation response 1. During adaptation to 3 per cent CO₂ and 2. of the high and low ventilation groups. Printed with permission of the *Journal of Applied Physiology*

DEADSPACES, RESPIRATORY PATTERN AND RESPIRATORY RESPONSE TO CO₂

Table 1 contains data on deadspaces and arterial and alveolar P_{CO₂} and P_{O₂} gradients obtained from ten subjects from whom arterial samples were collected.

Table 1. *Deadspace and Arterial-Alveolar P_{CO₂} and P_{O₂} Gradient in Chronic Respiratory Acidosis (10 Subjects)*

Condition	Control	40 days exp. to 1.5% CO ₂	9 day recovery on air	4 weeks recovery on air
Physiological deadspace (ml)	169	273*	262*	174
Physiological deadspace per cent Tidal Volume	29%	35%	37.6%	27%
Anatomical deadspace (ml)	157	214*	213*	163
Alveolar deadspace (ml)	12	59*	49*	10
Alveolar P _{CO₂} , mm Hg	38.2	39.6*	39.9	37.4
Arterial P _{CO₂} , mm Hg	39.4	44.9*	43.9*	38.3
Δ Arterial-Alveolar P _{CO₂} , mm Hg	1.3	5.3*	3.8*	8
Δ Arterial-Alveolar P _{O₂} , mm Hg	10.6	24.9*	20.3*	13.4

* Statistically Significant

Anatomical deadspace rose during CO₂ exposure from 28 per cent of tidal volume to 33-35 per cent which suggests a dilatory effect of CO₂ on the airways. Physiological deadspace, alveolar deadspace and Pa-P_ACO₂ gradient, as well as P_AO₂-PaO₂ gradients increased during exposure to CO₂. These findings indicate an increase in unperfused and unventilated alveoli during prolonged exposure to CO₂. Severinghaus and Stupfel (1957) and Severinghaus, Stupfel and Bradley (1957) have shown that the alveolar deadspace increases with increasing tidal volume and that the arterial-alveolar CO₂ gradient has a positive correlation with alveolar deadspace. It seems, therefore, that subjects who normally have a large tidal volume while breathing air and show a low response to CO₂ will have a certain degree of alveolar deadspace.

The increase of alveolar deadspace found during chronic exposure to 1.5 per cent produces a buffering effect on the gas composition of the alveoli. If a certain percentage of alveoli are well ventilated but poorly perfused, the gas composition of the alveoli will be altered towards that of the deadspace gas as outlined by Ross and Farhi (1960), leading to a reduction of the alveolar P_{CO₂} and an increased arterial alveolar P_{CO₂} gradient. A large alveolar deadspace will produce and maintain a higher arterial CO₂ tension and a correspondingly larger buffer capacity (bicarbonate) in the arterial blood. If CO₂ is inhaled under these conditions a mechanical buffering of CO₂ in the lungs is combined with a chemical buffering in the blood which will effectively reduce the development of peak CO₂ tensions in arterial and mixed venous blood and thereby limit the respiratory response to CO₂.

The lower response to CO₂, found in subjects with a larger tidal volume, is related to several factors. Besides an increased deadspace ventilation mechanical factors play a role. Evidence for the influence of the latter has recently been furnished by Milic-Emili and Tyler (1963) who demonstrated a linear relationship between alveolar CO₂ tension and the rate of mechanical work of inspiratory muscles. Moreover, the effort required by the inspiratory muscles to maintain a given level of pulmonary ventilation increases with increasing tidal volume because of the greater amount of elastic work involved (Otis, 1954). Since the rate of work is the same for the same deviation of P_ACO₂, it was concluded that an increased tidal volume would have to result in a reduction of the ventilatory response to CO₂ (Milic-Emili and Tyler, 1963).

Table 2. Ventilatory Response to 5 per cent CO₂ before, during and after Exposure to 1.5 per cent CO₂ over a Period of 42 Days, 21 Subjects

		1	2	3
		Test in submarine during control period on air	Test in submarine after 40 days exposure to 1.5 per cent CO ₂	Test in laboratory 3 weeks after exposure to 1.5 per cent CO ₂
Total group of subjects	Mean	1/min BTPS 17.91	1/min BTPS 14.58*	1/min BTPS 18.91
respir.	S.D.	3.68	2.46	3.88
min. vol.	N	21	21	21
Low ventilation group	Mean	14.80	14.60	16.07
respir.	S.D.	2.69	2.76	3.49
min. vol.	N	7	7	7
High ventilation group	Mean	19.47	14.57*	20.33
respir.	S.D.	3.04	2.31	3.22
min. vol.	N	14	14	14

* Difference between results of Test No. 2 and Test No. 1 (control) statistically significant at the 1 per cent level and better

The ventilatory response to 5 per cent CO₂ measured after 35-41 days of exposure to 1.5 per cent CO₂ in 21 subjects is significantly depressed compared with control values prior to exposure and data obtained after four weeks recovery on air (Table 2). These results show a close parallelism to experiments after 3 per cent CO₂ exposure for three and six days, in which the same effect was observed (Haebisch, 1949; Schaefer, 1949). If the subjects are classified in a low and high ventilation group, according to the previously used procedure (Schaefer, 1958), it can be noted that the low ventilation group does tolerate the exposure to 1.5 per

cent CO_2 without significant depression of the ventilatory response to 5 per cent CO_2 (Table 2). These subjects must be already partially adapted to a higher CO_2 level before they are exposed to 1.5 per cent CO_2 and should show a respiratory pattern found to be associated with (1) the lowered response to CO_2 in acute conditions, and (2) respiratory acclimatization to CO_2 . Confirmatory evidence for this hypothesis is shown in Table 3.

Table 3. Respiratory Pattern of Low (A) and High (B) Ventilation Groups while Breathing Air Tested before, during and after Exposure to 1.5 per cent CO_2

	N	Test in submarine control period on air	Test in submarine, 40 days exposure to 1.5 per cent CO_2	Test in laboratory 4 weeks after exposure to 1.5 per cent CO_2
Group A: low ventilation group				
Respiratory rate	7	8.0 (2.3)	8.0 (2.0)	7.6 (1.4)
Tidal volume, ml (BTPS)	7	820 (260)	827 (290)	741 (170)
Group B: high ventilation group				
Respiratory rate	14	10.5* (2.1)	10.1 (3.4)	11.2* (3.0)
Tidal volume, ml (BTPS)	14	634 (190)	660 (220)	652 (260)

* Differences between two groups statistically significant at the 5 per cent level and better

HISTOPATHOLOGICAL STUDIES ON LUNGS OF ANIMALS IN CHRONIC HYPERCAPNIA

Histopathological studies on guinea pigs exposed to 1.5 per cent CO_2 , 3 per cent CO_2 and 15 per cent CO_2 for prolonged periods showed the development of atelectasis and hyaline membrane formation in subpleural regions during exposure to 3 per cent CO_2 and 15 per cent CO_2 . Incidence of both hyaline membranes and atelectasis decreased during the compensatory phase of CO_2 exposure, suggesting an adjustment of gas exchange and blood flow during this period (Niemoeller and Schaefer, 1962). Evidence for a direct effect of CO_2 on the mitochondria of alveolar lining cells, resulting in a decrease of surface active material, has recently been found in guinea pigs exposed to 15 per cent CO_2 (Schaefer, Avery and Bensch, 1964).

ACID BASE BALANCE AND ELECTROLYTE SHIFTS

In chronic respiratory acidosis induced by prolonged exposure to 1.5 per cent CO₂, some characteristic changes occur in electrolytes. Mention is made only of the cation exchange in the red cells, as an indication of CO₂ adaptation. The red cells showed an increase of sodium, after 35-41 days of exposure to CO₂ and during 8 to 9 days of recovery on air, that was associated with an approximately equivalent reduction of potassium in the red cells (Schaefer, 1964) (Table 4).

Table 4. *Erythrocyte Cation and Anion Exchange in Chronic Respiratory Acidosis (10 Subjects)*

Condition	Control	35-41 days exposure to 1.5 per cent CO ₂	9 days recovery on air	4 weeks recovery on air
Na, mEq/L Red Cells	13.5	21.6*	24.4*	12.8
K, mEq/L Red Cells	86.0	78.9*	76.2*	79.9
HCO ₃ , mMol/L Red Cells	14.3	17.0*	17.0*	16.3*
CL, mEq/L Red Cells	55.8	58.3	56.9	58.8

* Statistically significant

A similar shift of sodium into the red cells and an associated potassium loss was found clinically in cases of respiratory acidosis combined with decompensation and congestive heart failure (Buckley and Siecker, 1961).

ADAPTATION PROCESSES TO BREATH-HOLD DIVING

Since the skin diver is exposed to rather high CO₂ tensions and low O₂ tensions during the breath-hold dive (Schaefer and Carey, 1962) (Figs. 4, 5), one would expect to find an adaptation to high CO₂ and low O₂.

The ventilatory response to 10.5 per cent CO₂ was measured in a group of laboratory personnel serving as controls and instructors at the Espace Training Tank and found significantly reduced in the latter group. Moreover, the trained divers (instructors) showed a better oxygen utilization (low ventilation per liter oxygen uptake) and accepted a significantly larger debt during 33 min of exposure to 10.5 per cent O₂ than the group of laboratory personnel (Schaefer and Alvis, 1951).

The CO_2 tolerance curves were obtained by exposing subjects for 15 min to 3.3, 5.4, and 7.5 per cent CO_2 . Alveolar ventilation and alveolar gas CO_2 tensions were determined at the end of each exposure period. The stimulus response curves (or tolerance curves) to CO_2 showed, in the case of the tank instructors, a shift to the right and a decreased slope (Schaefer, 1955 and Schaefer *et al.*, 1952). The high tolerance to CO_2 is developed during the diving period and lost after a three-month layoff

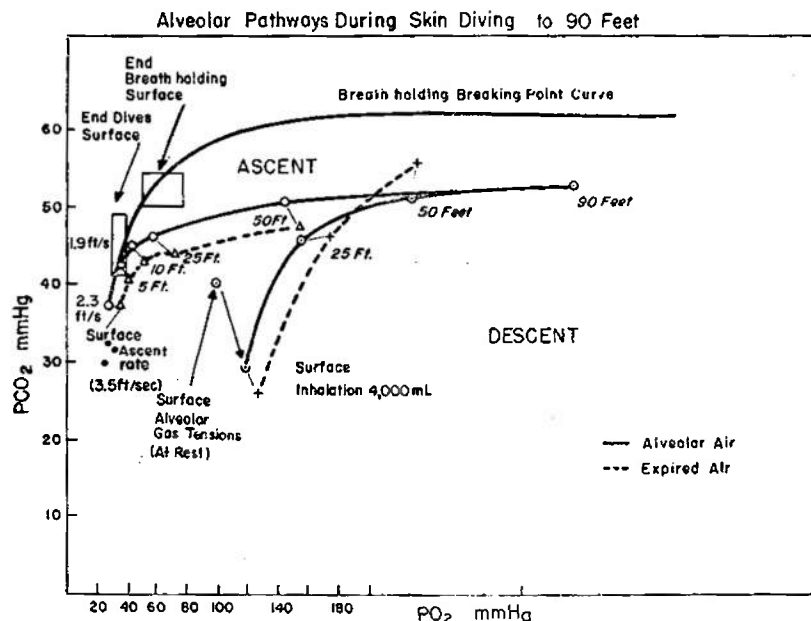


FIG. 4. Alveolar pathways during breath-holding dives to 90 ft showing reversed CO_2 gradient. At 50 ft P_{CO_2} mixed expired air is 6 mm Hg higher than P_{CO_2} "alveolar air." Surface breath-holding breaking point curve drawn for comparison with diving breath-holding curve. End dive alveolar P_{CO_2} decreased with increasing rate of ascent reaching 30 mm Hg at 3.5 ft/sec. Printed with permission of *Science*

period as shown in CO_2 sensitivity tests in eight tank instructors (Schaefer, 1961). Blood gas and electrolyte changes observed at the end of a longer period of water work were similar to those noted during adaptation to prolonged exposure to CO_2 (Schaefer, 1963). They consisted in a decrease in pH, increase in P_{CO_2} and bicarbonate levels commensurate with an increase in hematocrit and a red cell cation exchange, e.g. increase in red cell sodium and decrease in red cell potassium. These adaptive changes disappeared after a 3-month layoff period (Schaefer, 1961). Evidence of an increase in CO_2 stores, as the result of diving, was recently obtained in instructors following a two-year period of water work when compared with data obtained after a 3-month layoff period (Dougherty and Schaefer, 1962). During constant hyperventilation, lasting for one hour, more CO_2 was eliminated and the

end tidal CO₂ tension was significantly elevated under the first condition. The decreased sensitivity to CO₂ and low O₂ found in skin divers represents an adaptation similar to that observed in diving animals (Irving, 1939).

The lung volumes of divers were also found to change during prolonged training (Carey, Schaefer and Alvis, 1956). A longitudinal study was carried out and the lung volumes of tank instructors measured at the beginning of their tour of duty and after one year. Inspiratory reserve, tidal volume, vital capacity, and total

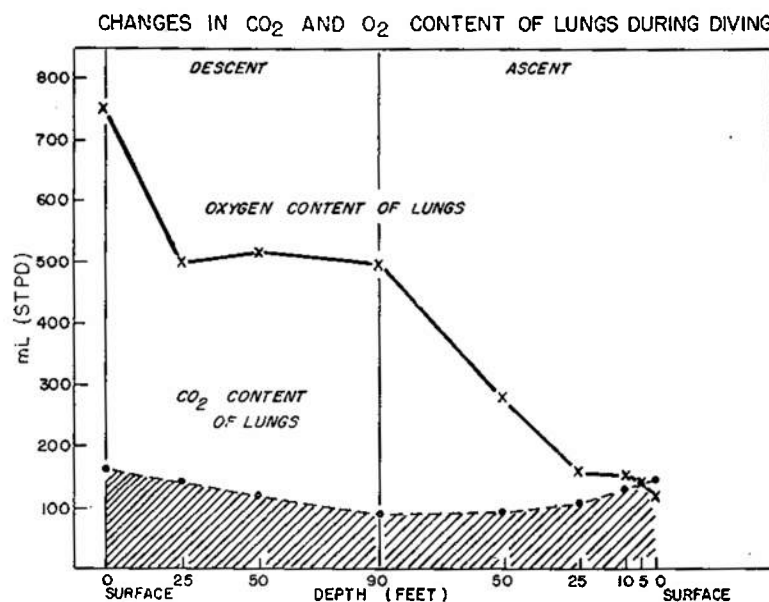


FIG. 5. CO₂ and O₂ content of lungs during diving (milliliters, STPD) calculated from measured gas tensions and volumes of mixed expired and alveolar air at various depths, the known residual volume and the total dry gas pressure in the lungs. Printed with permission of *Science*

capacity showed a significant increase while residual capacity decreased. The maximum average depth a diver can reach without getting a thoracic squeeze depends on the ratio of total lung capacity to residual capacity and the volume of the airways. The observed change in his ratio results in a 20–30 ft extension in the maximum safe depth after one year of duty. The changes in lung volumes, consisting of an increase in total lung capacity, vital capacity and tidal volume, and decrease in residual volume, might contribute to the reduced sensitivity to CO₂ because of the relationship found between large tidal volume, slow respiratory rate and low response to CO₂ (Schaefer, 1958).

ADAPTATION TO SCUBA AND DEEP SEA DIVING

Scuba Diving

Using open or closed circuit Self Contained Under Water Breathing Apparatus (SCUBA) units at a greater depth, the direct effect of pressure produces an increased density of the breathing mixture resulting in an increased breathing resistance. Under these conditions, the work of breathing was found decreased in both breathing apparatus and in the airways of the diver (Mead, 1955, Marshall, Lanphier and DuBois, 1956). Pulmonary resistance at 4 atmospheres pressure increased two-fold compared with the values at sea level (Mead, 1956). Froeb (1961) compared the respiratory response to CO_2 in 16 professional divers using SCUBA equipment with those of non-divers and did not find any evidence of adaptation to CO_2 in the SCUBA divers. In studies of well trained underwater swimmers of the U.S. Navy Underwater Demolition Team (UDT) and untrained swimmers (laboratory personnel), using a closed circuit oxygen breathing apparatus, a higher mean end tidal P_{CO_2} tension was found in the trained swimmers during dives at a speed of 1.1 to 1.8 km/hr (Goff, 1957). For resting conditions underwater, differences were insignificant. The end tidal P_{CO_2} values of the trained swimmers ranged from 46.2 to 52.1 mm Hg as compared with 37.4 to 38.5 mm Hg in the control group. The higher end tidal P_{CO_2} values of the UDT men were found to be associated with a better oxygen utilization as indicated in the lower oxygen equivalent of 19.1 to 20 liters ventilation per liter of O_2 uptake compared with 21.3 to 24.6 in the controls. The trained swimmers showed a characteristic breathing pattern of slow deep breaths with long post-inspiratory pauses. They also had a larger tidal volume than the control group. These findings indicate a measure of CO_2 adaptation similar to that found in skin divers reported above.

Furthermore, adaptation to an increased work of the inspiratory muscles might have contributed to the elevated P_{CO_2} in the trained underwater swimmers because it was shown that the alveolar P_{CO_2} increases linearly with the workload of the inspiratory muscles (Milic-Emili and Tyler, 1963).

Deep Sea Diving

In deep sea diving ("Hard Hat Diving"), in which the conventional suit and helmet are used, a large amount of air has to be ventilated to prevent an accumulation of CO_2 . Often this may not be fully accomplished. Moreover, at greater depths, breathing resistance becomes very marked and might easily lead to CO_2 retention. Lanphier found that a considerable number of experienced deep sea divers at the U.S.N. Experimental Diving Unit showed a retention of CO_2 during underwater work (1955a, b). The respiratory minute volume declined during work dives to moderate depth using oxygen-nitrogen mixtures. The degree of retention of carbon dioxide was found to be related to the ventilatory response to CO_2 (Lanphier,

1956). When breathing resistance was reduced by the use of helium-oxygen mixtures, the CO₂ retention was small or absent.

A more detailed account of adaptation in diving has been given elsewhere (Schaefer, 1965).

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